Journal of
Cardiology & Cardiovascular
Surgery

Original Article

DOI: 10.51271/JCCVS-0047

The relationship between obesity paradox and C-reactive protein in patients with ST-segment-elevation myocardial infarctions

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Cite this article: Arslan GY, Toprak C, Karataş M, Soner S. The relationship between obesity paradox and C-reactive protein in patients with ST-segment-elevation myocardial infarctions. *J Cardiol Cardiovasc Surg.* 2025;3(1):1-4.

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Received: 28/02/2024 ◆ **Accepted**: 12/12/2024 ◆ **Published**: 27/03/2025

ABSTRACT

Aims: Inflammation plays a very important role in the pathogenesis of coronary artery disease (CAD) and its prognosis. Especially; C-reactive protein (CRP) is associated with poor prognosis in patients with CAD. In this study, the relationship between CRP levels and body-mass index (BMI) was investigated in patients who underwent primary coronary intervention (PCI) due to ST-segment elevation myocardial infarction (STEMI).

Methods: Between January 2015 and February 2016, 132 patients who underwent PCI due to acute STEMI were included in the retrospective study. Patients were classified into two groups: (group 1:BMI <25kg/m^2 n:27 and BMI >35 kg/m^2 n:9, total:36 patients; group 2: 25<BMI<30 kg/m^2 n:58 and 30<BMI<35 kg/m^2 n:38, total 96 patients). Class 2, 3 obese patients and normal weight patients constituted group 1 whereas pre-obese and class 1 obese patients were included in group 2. The patients are grouped in this way because the prognosis of the first group is worse in obesity paradox studies.

Results: CRP was found to be significantly lower in STEMI patients with 25>BMI<35. Whereas it was significantly higher in STEMI patients with 25<BMI>35.

Conclusion: In this study, the relationship between CRP levels and BMI was investigated in patients who underwent PCI due to STEMI. The reasons for the better prognosis of mildly overweight and class 1 obese patients with STEMI diagnosis may be the low values of CRP which has many effects on atherosclerotic plaque formation.

Keywords: ST-segment elevation myocardial infarction, C-reactive protein, obesity paradox

INTRODUCTION

The prevalence of obesity has increased significantly worldwide, becoming a major health and social problem.[1] Obesity is associated with increased risks of hypertension, metabolic syndrome, and type 2 diabetes mellitus, all strong risk factors for coronary artery disease (CAD).[2,3] Despite these adverse cardiovascular effects of obesity, numerous studies have revealed better cardiovascular outcomes in obese individuals which is defined as 'obesity paradox'.[4-6] The aetiology of obesity paradox remains largely unexplained.

Weight that is higher than what is considered as a healthy weight for a given height is described as overweight or obese. Body-mass index (BMI) is used as a screening tool for overweight or obesity. According to the World Health Organization (WHO); BMI was categorized as follows: underweight (BMI<18.5 kg/m^2), normal (BMI 18.5≤24.9 kg/m^2), overweight (BMI 25≤30 kg/m^2), and obesity (BMI≥30 kg/m^2). Obesity is classified as class I for a BMI between 30 and 34.9 kg/m^2, class II for a BMI between 35 and 39.9 kg/m^2, and class III for a BMI≥40 kg/m^2.

Inflammation plays a very important role in the pathogenesis of CAD and its prognosis.[7] Especially; many clinical studies indicate that C-reactive protein (CRP) is associated with poor prognosis in patients with CAD.[8]

In this study, the relationship between CRP levels and BMI was investigated in patients who underwent primary coronary intervention (PCI) due to ST elevation myocardial infarction (STEMI).

METHODS

The study was conducted with the permission of Health Sciences University Gazi Yaşargil Training and Research Hospital Clinical Researches Ethics Committee (Date: 12.12.2024, Decision No: 268). Between January 2015 and February 2016, 132 patients who underwent PCI due to acute STEMI were included in the retrospective study. The confidential information of the patients was protected according to current national normative. The study protocol

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was approved by the ethics committee and Helsinki Declaration.

ACS with ST segment elevation was defined as the presence of chest pain with persistent ST-segment elevation of at least 0.1 mV in at least two contiguous leads or a new left bundle-branch block.

Major exclusion criteria included cardiogenic shock, clinically significant hepatic disease, infection, patients who were followed-up by non-PCI medical treatment, and CRP>10 mg/dl. This study evaluated demographic characteristics, risk factors and laboratory findings. Patients were classified into two groups: (group 1: BMI<25kg/m² n:27 and BMI>35 kg/m² n:9, total:36 patients; group 2: 25<BMI<30 kg/m² n:58 and 30<BMI<35 kg/m² n:38, total 96 patients). Class 2,3 obese patients and normal weight patients constituted group 1 whereas pre-obese and class 1 obese patients were included in group 2. The patients are grouped in this way because the prognosis of the first group is worse in obesity paradox studies.[4-6] The characteristics of the patients consisted of medical history (diabetes mellitus, hypertension, hyperlipidemia, previous myocardial infarction, smoking, family history), the laboratory findings (glucose, creatinine, cardiac enzymes, serum cholesterol, CRP, hemoglobin, hematocrit, leukocyte, lymphocyte, neutrophil, mean platelet volume, platelets, albumin, total protein, bilirubin and left ventricular ejection fraction (LVEF).

Statistical Analysis

Numerical variables were mean±standard deviation; categorical variables were frequency and percentage. Patients were divided into 2 groups according to BMI. The student-t test was used to compare normal distribution variables and the Mann-Whitney U test was used to compare non-normal distributions. Chi-square test was used to compare categorical variables. Patients were divided into 4 groups according to BMI and one way analysis of variance (ANOVA) was applied to compare CRP values. SPSS 16.0 (Statistical Package for Social Sciences) program was used for statistical analysis of the data in the study. p value<0.05 was considered statistically significant for all tests.

RESULTS

The demographic characteristics of 132 patients' (115 men, 17 women), risk factors, laboratory results are listed in **Table 1**. There was no difference between two groups according to history of coronary artery disesase and three vessels disease. There was no statistically significant difference between the two groups regarding demographic features, risk factors and LVEF (**Table 2**). Total cholesterol (192.50±43.99; 175.30±41.22, p=0.044), hemoglobin (13.92±1.40; 13.23±1.98, p=0.026), hematocrit (42.42±4.19; 40.51±5.61, p=0.037) and triglyceride (179.59±99.13; 140.25±53.12, p=0.026) levels were significantly higher in group 2 compared to group 1. On the other hand, CRP was significantly higher in group 1 (p=0.004) (**Table 3**). Subgroup analysis was performed to assess CRP according to the patients' BMI. Patients were divided into 4 subgroups according to BMI: subgroup 1 BMI<25 (n:27), subgroup 2 25<BMI<30 (n:58), subgroup 3 30<BMI<35 (n:38), subgroup 4 BMI>35 (n:9). The mean CRP values of the subgroups are given in **Table 4**. The distribution of CRP values according to BMI is shown in **Figure**. There was no statistically significant difference between CRP values of the subgroups. CRP was found to be significantly lower in STEMI patients with 25>BMI<35.Whereas it was significantly higher in STEMI patients with 25<BMI>35.

Table 1. Baseline demographics and medical history of the study population

	Group 1 BMI>35 and BMI<25 (n=36)	Group 2 35≥BMI>25 (n=96)	p value
Patient characteristics			
Age years	59.5±9.82	54.3±12.2	0.250
Gender, male, n	31	84	0.518
BMI (kg/m²)	26.2±6.0	28.8±2.3	0.015
Diabetes mellitus, n	13	32	0.459
Hypertension, n	14	41	0.423
Dyslipidaemia, n	12	40	0.252
Smoker (current), n	16	42	0.679
Smoker (ex), n	13	29	0.392
Chronic kidney disease, n	6	8	0.143
Previous CAD history, n	10	19	0.224
Family CAD history, n	14	50	0.124
Anterior MI, n	19	67	0.476
Three vessels, n	8	16	0.678

BMI: Body-mass index, CAD: Coronary artery disease, MI: Myocardial infarction

Table 2. Laboratory results of the study population

	Group 1 BMI>35 and BMI<25 (n=36)	Group 2 35≥BMI>25 (n=96)	p value
Laboratory data			
CRP (mg/dl)	1.88±2.14	0.75±0.81	0.004
Haemoglobin	13.23±1.98	13.92±1.40	0.026
Haematocrit	40.51±5.61	42.42±4.19	0.037
Leukocyte	12.86±3.12	12.29±3.78	0.423
Lymphocyte	1.96±0.87	1.94±0.92	0.906
Neutrophil	10.01±3.42	9.57±3.65	0.446
Mean thrombocyte volume (MPV)	8.34±0.96	8.62±1.03	0.159
Thrombocyte	238.58±47.02	234.48±52.97	0.685
Neutrophil/lymphocyte ratio	7.07±5.79	5.98±3.28	0.295
LDL	112.36±35.49	121.08±38.15	0.236
HDL	36.11±7.59	38.23±8.85	0.204
Triglyceride	140.25±53.12	179.59±99.13	0.026
Total cholesterol	175.30±41.22	192.50±43.99	0.044
Glucose	163.47±63.27	168.97±84.01	0.722
Urea (mg/dl)	38.96±22.75	33.75±10.46	0.193
Serum creatinine (mg/dl)	0.99±0.62	0.81±0.24	0.115
Initial troponin	15.28±25.97	19.21±29.51	0.482
Bilirubin	0.64±0.32	0.60±0.32	0.512
Albumin	3.69±0.44	3.78±0.38	0.217
Total protein	6.43±0.59	6.42±0.48	0.943
LVEF	49.58±11.29	49.06±10.24	0.801

BMI: Body-mass index, CRP: C-reactive protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, LVEF: Left ventricular ejection fraction

Table 3. CRP values of the subgroups

	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4
CRP mg/dl	1.77±2.23	0.77±0.91	0.72±0.66	2.22±1.92

Subgroup 1: BMI<25, Subgroup 2: 25≤BMI<30, Subgroup 3: 30≤BMI<35, Subgroup 4: BMI≥35, CRP: C-reactive protein, BMI: Body-mass index

Table 4. Statistical relations of the subgroups with each other (p value)

	Supgroup 1	Supgroup 2	Supgroup 3	Supgroup 4
Supgroup 1	-	0.017	0.022	0.848
Supgroup 2	0.017	-	0.999	0.027
Supgroup 3	0.022	0.999	-	0.027
Supgroup 4	0.848	0.027	0.027	-

Subgroup 1: BMI<25, Subgroup 2: 25≤BMI<30, Subgroup 3: 30≤BMI<35, Subgroup 4: BMI≥35, BMI: Body-mass index

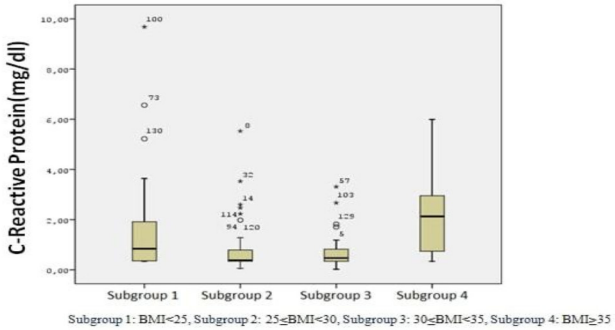

Figure. The distribution of CRP values according to BMI
CRP: C-reactive protein, BMI: Body-mass index

DISCUSSION

CAD is one of the most important causes of death in the world. Rupture of atherosclerotic plaques and plaque erosion in the coronary arteries cause acute coronary syndrome. CRP is an acute phase reactant that plays a role in atherosclerotic plaque formation and plaque rupture. The reference hs-CRP value has been found to be associated with a poor prognosis when measured >3 mg/L in stable CAD and >10 mg/L in acute coronary syndromes.[9] JUPITER and PROVE-IT clinical trials have shown that clinical outcome is better with low CRP in patients receiving statin therapy.[10,11] The relationship between inflammation and very weak and morbidly obese patients, who are reported to have poor prognosis for CAD, has been investigated in this clinical trial.

In the obesity paradox of CAD, overweight patients and type 1 obese patients have been shown to have a better prognosis than normal weight patients, type 2 and 3 obese patients.[12] When the long term results of STEMI patients over 65 age is evaluated, similar obese paradox is observed, the best prognosis is documented for moderately obese (30<BMI<35) group.[13]

CRP is an acute phase protein produced in liver cells in response to IL-6 and TNFa cytokines. It has been shown that CRP is also produced by the atherosclerotic intima layer.[14] It is highly sensitive, and may indicate nonspecific inflammation, tissue damage, and infection. Increased risk of cardiovascular disease has been detected in patients with increased inflammatory markers such as CRP, leukocyte, fibrinogen and IL-6.[15] Inflammatory cells, inflammatory proteins, and vascular cells inflammatory signals has an important role in pathogenesis of different levels of atherosclerosis including atheroma plaque accumulation, plaque instability, rupture, post angioplasty and restenosis.[16] In the buildup of stabilize plaque, it is shown that CRP is accumulated on LDL and causes macrophages to uptake more LDL and consequently causes them to transform into foam cells. There is a rich literature that shows the relationship between acute coronary syndrome and inflammation. One of the most investigated markers of inflammation in acute coronary syndromes is the CRP.[17,18] Oltrona et al.[19] discovered that CRP is an independent risk factor in AKS and a 30-day predictor of mortality. In a study with 1078 STEMI patients, CRP and WBC are recognized as independent in-hospital mortality predictors.[20] Another similar study claimed that CRP indicates the seriousness of infarct in STEMI and a predictor of complications.[21] High CRP levels is detected in thin-capsule atheroma plaque which is identified with OCT. This shows that inflammatory period takes an active role in plaque activation.[22] Correlated regression of CRP values after plaque formation stabilized by high dose statin administration at post STEMI proves that inflammation and consequently CRP are effective on motile plaque.[23] In our study, there was no statistical difference between the groups in terms of-inflammation markers except CRP. Significantly different levels of CRP among the groups may indicate that CRP-mediated inflammation may be one of the causes of obesity paradox. In the subgroup analysis, the distribution of CRP levels in groups was similar to the U-Shaped curve in previously reported obesity paradox studies.

Adiponectin secreted from adipose tissue stimulates fatty acid oxidation in skeletal muscle and inhibits glucose production in the liver, providing an improvement in whole-body energy homeostasis. Adiponectin is also a classic anti-inflammatory agent that reduces inflammation in various cell types by Adipo R1 and R2 signaling mechanisms. The anti-inflammatory, anti-hypertrophic and antiapoptotic properties of adiponectin cause vasculature, heart, lung and colon protection.[24,25] One study showed that adiponectin was inversely proportional to CAD progression and CRP was directly proportional.[26] Adiponectin levels were found to be reduced by abnormal glucose metabolism.[27] This suggests that adipose tissue can be protective by endocrine effect to a certain level. However, with the progressive deterioration of glucose metabolism in advanced stages of obesity, it may cause the complications of metabolic syndrome. Obesity complications are expected to be less frequent in overweight and type 1 obesity compared to type 2 and 3 obesity. As a result, the protective effects of adiponectin may be expected to be more prominent in overweight and type 1 obese patients. The anti-inflammatory effects of adiponectin may lead to decrease in CRP levels and suppression of CRP related tissue effects. One of the reasons for the worse survival rates of normal weight people may be the lack of cardio-protective effects of adipose tissue.

Limitations

First of all our clinical study are retrospective, single centered, and has small number of patients. Future studies may be needed.

CONCLUSION

CRP was found to be significantly lower in STEMI patients with 25>BMI<35. Whereas, it was significantly higher in STEMI patients with 25<BMI>35. One of the reasons for the better prognosis of mildly overweight and class 1 obese patients with STEMI diagnosis may be the low values of CRP which has many effects on atherosclerotic plaque formation.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of Health Sciences University Gazi Yaşargil Training and Research Hospital Clinical Researches Ethics Committee (Date: 12.12.2024, Decision No: 268).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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